B

BACTERIOLOGY AND MICROBIOLOGY. The science known as bacteriology or microbiology came into existence when the French chemist Louis Pasteur, the German physician Robert Koch, and their associates established the role of specific microorganisms in causing specific fermentations and diseases. Yet the full significance of the new science they wrought extends well beyond providing the evidence to support and the tools to apply what their medical contemporaries called "germ theory." Bacteriology was less a new discipline with its own set of research problems than a new kind of laboratory or experimental system in which myriad physiological, chemical, and biological problems could be addressed and from which new sciences could emerge, notably immunology. Moreover, the development of bacteriology was nearly inseparable from the role it played in wider material, social, and conceptual transformations that unfolded in and beyond the industrializing world in the century after 1860.

Ever since the seventeenth century, the learned and the curious had bent over microscopes to peer at a hitherto unseen new world that seemed to teem with life. These visions inspired everything from philosophical systems by Gottfried Wilhelm Leibniz to comical verse by Jonathan Swift to natural history of "animalcules" and "infusoria" and controversy over the origin of life. By the mid-nineteenth century, field observation and innovation by men like the physician Ignaz Semmelweis in the maternity clinic, the civil servant and amateur agronomist Agostino Maria Bassi on the silk plantation, and the surgeon Joseph Lister were yielding the first testable conjectures concerning the role of microscopic life in processes of putrefaction and disease.

A pencil drawing by artist Alfons Mucha of Louis Pasteur

Decisive in the transition from this field experimental work to systematic laboratory study of a wide range of specific microorganisms grown in artificial media under controlled conditions were, first, application of chemistry and experimental physiology to the study of apparently "germ"-related processes and, second, radical innovation in methods and materials. The first of these phases, roughly 1835–1875, began in the Berlin physiology laboratory of Johannes Peter Müller. His student Theodor Schwann designed an experimental apparatus allowing him to observe that putrefaction and alcoholic fermentation occurred only in the presence of air that had not been heated to destroy any microscopic life it contained.

Schwann published one important paper and then moved on to other research; twenty years later Louis Pasteur extended Schwann's work to other fermentations and to disease, publishing hundreds of papers and numerous books, training students and gathering associates into his laboratory and thus establishing a school of research on microscopic organisms. Whereas his forerunners and contemporaries were unable to observe microorganisms in isolation from complex natural media such as grape juice, beer, and blood, the chemist Pasteur created a general experimental system for cultivating microorganisms in artificial media. These media were chemically calibrated and their environments controlled so as to favor the growth of any given species over others, thus allowing each to be studied in isolation, its chemical input and output subjected to exact analysis.

The second phase in the emergence of bacteriology, roughly 1875–1890, is associated especially with Robert Koch. The methods and instruments of chemistry and physiology were supplemented and often replaced by novel ways of cultivating, manipulating, and representing microorganisms. Thus the delicate blown-glass globe taken from chemistry by Schwann and Pasteur for use in growing microbial cultures—tricky to manage and precarious to transport, filled with infusions difficult to maintain in biological purity and impossible to scan with the microscope—became the simple, transportable, scannable glass dish named after Koch's associate Richard Petri, now ubiquitous in biomedicine, with its conveniently immobile growing-surface of gelatine or agar-agar, upon which a mixed culture could be sown and then divided into colonies or individual bacteria to be "isolated" and replated as "pure cultures." Whereas Pasteur's difficult methods had been adopted by a mere handful of investigators outside his laboratory, now the new bacteriological technique spread throughout the world.

diseases in showing the direct relevance of the laboratory to understanding events in the field. Koch watched the seemingly static "little rods" (bacilli) observed by other microscopists in anthrax blood multiply by division and, in a characteristic life-cycle, change form into highly resistant spores. The spore stage explained the ability of the disease to persist in abandoned pastures. Second, Koch showed that the welter of microscopic life that others had observed in infected wounds could be resolved into a limited number of species, each correlated with a distinct set of pathological effects. Finally, in the work that made him virtually a household name, Koch used his new method of solid-media culture to isolate a microscopic species responsible for the leading cause of death in the Western world, pulmonary consumption or tuberculosis, as well as for the dread disease cholera, while his students Friedrich Loeffler and Georg Gaffky did the same for diphtheria and typhoid fever.

Though these and similar demonstrations are often thought of as the end of etiological research, they were in fact its beginning. By what mechanisms and under what circumstances did microorganisms cause disease and epidemics? Why did some people exposed to infection become ill while others did not? Some early bacteriologists avoided these difficult questions. Others explored them through work on variable virulence, secreted toxins, and, above all, natural and acquired immunity.

In 1880, Pasteur's invention of artificial vaccines launched the study of immunity and immunization. But it also made bacteriology something it had not been before, namely, experimental biology in the strict sense: experimental study of species, inheritance, variation, and the Darwinian evolutionary mechanism of natural selection. Pasteur's vaccines were weakened cultures of pathogenic species, and many bacteriologists understood this weakening or "attenuation" to be biological variation. In the twentieth century, the study of microbial variation and of the associated phenomenon of infection of bacteria by virus (bacteriophage) came to have momentous theoretical consequences for the life sciences through its central role in the origins of molecular biology and genetics.

From its earliest, dramatic achievements, bacteriology was an icon of the triumph of technical skill and experimental discipline over speculation and superstition. Yet as some bacteriologists themselves pointed out, bacteriological research has also been shaped by myths and beliefs concerning purity and danger, life and death: disease-causing germs as demons or enemies, the seeds of disease and the soil of the body, the body as an armed citadel. The scope of meanings of microbiological research has continued ever since to range from the mundane (the quality of beer and the safety of milk) to the cosmic (the origin of life and the cycle of matter) to the political and social (relative importance of "seed" and "soil," or germs and social conditions, in disease causation).

Alongside these wider meanings, the rise of bacteriology involved a conceptual transformation in medicine: from defining diseases by their circumstances, symptoms, and pathologies to defining them by their causes; from clinical and pathological to etiological definitions of disease. Bacteriology gave medicine and hygiene powerful reasons for focusing on the identification and control of necessary, specific causes.

With the conceptual transformations came practical ones. Through bacteriology, not only could diseases be defined and understood in etiological terms, but they could be routinely diagnosed and sometimes even treated according to their causes rather than their symptoms. Bacteriological and serological testing put laboratories, for the first time, at the very center of everyday medical and public health practice. The emergence of routine bacteriological diagnosis in hospitals and municipal health departments may be the single most important event in the wider and longer history by which the means and authority of diagnosis, which once lay solely in the skilled and experienced hands of the physician, was increasingly placed in laboratories and machines.

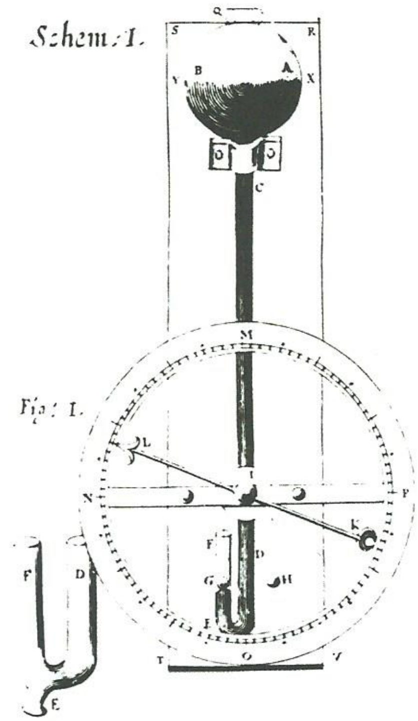
Beyond the laboratory revolution in medicine, bacteriological methods such as testing of bodies and waters and wastes, products such as vaccines, and technologies such as pasteurization remove the fabric of everyday human existence, consumption, and material production in and beyond the industrializing world. The immediacy of this impact has been unparalleled among the life sciences and comparable to the changes in civilization associated with electromagnetism and synthetic chemistry.

With its array of products and services, the bacteriological laboratory ushered in an era in the history of science in which experiment is often synonymous with invention, inquiry with application. The intimate and constant interaction of Pasteur, Koch, Paul Ehrlich, and others with government and business became a compelling model for the organization of scientific life in the twentieth century. The establishment of the Pasteur Institute in Paris (1888), Koch's institute in Berlin (1891), the Lister Institute in London (1891), Ehrlich's institute in Frankfurt (1899), and the Rockefeller Institute in New York (1901) inaugurated a new kind of large, national, nonuniversity research institution and an expansion in the scale and social role of the sciences of health and life, their growth into an omnipresent complex involving industry, commerce, philanthropy, the state, and the consumer.

ANDREW MENDELSOHN

BAROMETER. The barometer grew out of practical hydrostatics in the early seventeenth century. Italian mining and hydro-engineers had noticed that pumps would not raise water more than about thirty feet. Galileo proposed that "the force of the vacuum" could hold up a column of water only so tall in a pump before it broke, as if the vacuum were a rope holding up a weight. Isaac Beeckman, Giovanni Baliani, and others argued that the weight of the air outside the pump balanced the water column. Around 1641 Gasparo Berti attached a forty-foot lead pipe to the side of his house, filled it with water, sealed the top, and opened a cock at the bottom, which stood in a large vessel of water. Ten feet of water flowed out, leaving a column suspended some thirty feet high and a space above it that posed a difficult puzzle, since the reigning Aristotelian physics held the vacuum to be an impossibility.

Galileo's disciples repeated Berti's experiment with different liquids until, in 1644, Evangelista Torricelli filled a glass tube with mercury, inverted it in a bowl of the same liquid, and watched the silver liquid fall. Torricelli reasoned from the equality of the ratios of the heights of the mercury and water columns and their specific weights that the atmosphere indeed balanced the standing column. He suggested that his instrument "might show the changes of the air," but the meteorological possibilities of the instrument were largely ignored during two decades' debate over the nature of the space above the mercury and the balancing act of the air. The "Torricellian experiment" remained an experiment for the demonstration and investigation of the vacuum. Blaise Pascal pushed the experiment further towards a measuring



Wheel barometer designed by Robert Hooke (1635–1703) and depicted by him in his pioneering *Micrographia* (1665)

instrument by fitting the tube with a paper scale and watching the mercury travel "up or down according as the weather is more or less overcast." This arrangement he designated a "'continuous experiment,' because one may observe, if he wishes, continually." The word "barometer" appeared in 1663 in the work of Robert Boyle, who with Robert Hooke had set a tube in a window for weather observation.

Soon many new types of barometers appeared: siphon instruments, in which a recurved lower end replaced the barometer's cistern; double and triple barometers, in which successive liquids magnified the motions of the column; diagonal barometers, whose inclination had the identical function; and others. Many designs aimed at a growing market for philosophical and mathematical instruments among the well-to-do. None increased the barometer's accuracy, which did not concern natural philosophers of the seventeenth and early eighteenth centuries.

Precision became important after the Seven Years' War. European states inaugurated national cartographic projects to provide accurate topographic information for military campaigns, taxation, agricultural reform, and other programs of the late Enlightenment. Barometers provided a convenient, if not the most authoritative, method for measuring heights on these surveys, and a demand arose for their precision. The instruments also proved useful to scientific travelers and for investigations into the properties of the air at a time when philosophers were discovering the different gases constituting it and puzzling over water vapor and its pressure in the atmosphere. The Genevan natural philosopher Jean André Deluc, an avid Alpine explorer, designed the first barometer capable of precise measurement. Deluc's exhaustive *Recherches sur les modifications de l'atmosphère* (1772) included such reforms as boiling the mercury to remove dissolved air, methods for leveling the barometer and for reading the mercury meniscus, and corrections for the expansion with temperature of mercury, glass, and the ambient air. Equally important, Deluc showed how to deploy the instrument in repeated series of exhaustive measurements—a revolutionary technique. Deluc's rule for converting barometric measurements to heights was quickly adopted in England, where a national geodetic survey was underway.

In England, instrument makers, moving away from craft-based organization, implemented industrial techniques such as division of labor, machine manufacture, and research and development financed out of profits from government trade. By 1770, Jesse Ramsden, the most advanced among them, was manufacturing barometers accurate to one-thousandth of an inch. In France, the guilds hobbled efforts by the enlightened monarchy to modernize the instrument trade, though a few excellent instrument makers worked there towards the end of the ancien régime. The dissolution of the guilds during the Revolution and the need for instruments for military purposes and for metrification strengthened the instrument trade in France. Jean Nicolas Fortin's barometer, accurate to two-thousandths of an inch, became the standard model in France.

In the nineteenth century, the popularity of scientific travel and the increasing reach of European imperialism favored the development of the aneroid barometer. At the end of the seventeenth century, Leibniz had suggested an instrument that would balance the pressure of the atmosphere against a spring-loaded, flexible bellows or box. In 1844, Lucien Vidie developed a practical barometer based on this principle. The aneroid became popular among mountaineers and mariners; in the twentieth century, aviation pushed the development of highly accurate aneroid instruments.

The requirements of networks of weather observers organized by national governments in the late nineteenth century helped create a new class of barometers: the high-precision "primary" barometer, against which observers' instruments were calibrated. Manufacturers employed sophisticated methods, including the Sprengel mercury vacuum pump, to clean, fill, and evacuate these instruments.

THEODORE S. FELDMAN

BIOCHEMISTRY is the name most commonly used during the twentieth century to designate the branch of science that investigates the chemical constituents of living matter, the substances produced by organisms, the functions and transformations of these substances within organisms, and the energetic changes associated with them. Many of these topics had been studied under such names as iatrochemistry, animal and plant chemistry, and physiological chemistry.

From the time that chemistry itself emerged as a distinct investigative activity during the seventeenth century, chemical knowledge was regularly applied to the study or explanation of processes occurring in living organisms. The successive stages of digestion and the formation of blood came to be interpreted as a series of interactions of acids and alkalis when their study became prominent in the middle of the century. Alcoholic fermentation, which was often characterized as an "intestine motion," also became a model for the explanation of internal vital processes. Van Helmont was the first of many to suggest that "ferments" caused digestion and other transformations. During the seventeenth and eighteenth centuries, chemists divided their field into three parts according to the three kingdoms of nature. Substances obtained from the animal kingdom were characterized by "volatile alkali," an alkali that sublimed or passed over into the receiver in the distillation procedures central to early chemical analysis. Plant material contained, instead, predominantly fixed alkali. This distinction led to various concepts of nutrition during the eighteenth century, such as that proposed by Herman Boerhaave, who inferred that food entered the body in an "acidescent" condition, gradually becoming "alkalescent" as it transformed into blood, tissues, and eventually excretory products.

The changes in chemistry associated with the chemical revolution at the end of the eighteenth century also marked a transformation in the study of the chemical processes of life. Antoine-Laurent Lavoisier made three central contributions. Through the extension of his studies of combustion to several representative plant substances, especially sugar and oils, he showed that plant matter comprises carbon, hydrogen, and oxygen, individual substances being distinguished by the proportions in which they contain these elements. Drawing on the demonstration by his colleague, Claude Louis Berthollet, that "volatile alkali" is composed of nitrogen and hydrogen, Lavoisier concluded that animal substances contain four elements—carbon, hydrogen, oxygen, and nitrogen. By this time, chemists understood that "animal substances" did not derive from the animal kingdom alone, but constituted a class of substances, including fibrin, albumin, casein, and gluten, some of which came from plant matter.

Adapting his quantitative methods to the study of alcoholic fermentation, Lavoisier showed that the chemical change involved is the conversion of sugar to alcohol and carbonic acid. Determining the elementary composition of each of the substances involved, he produced the first balanced chemical equation for a biologically important process.

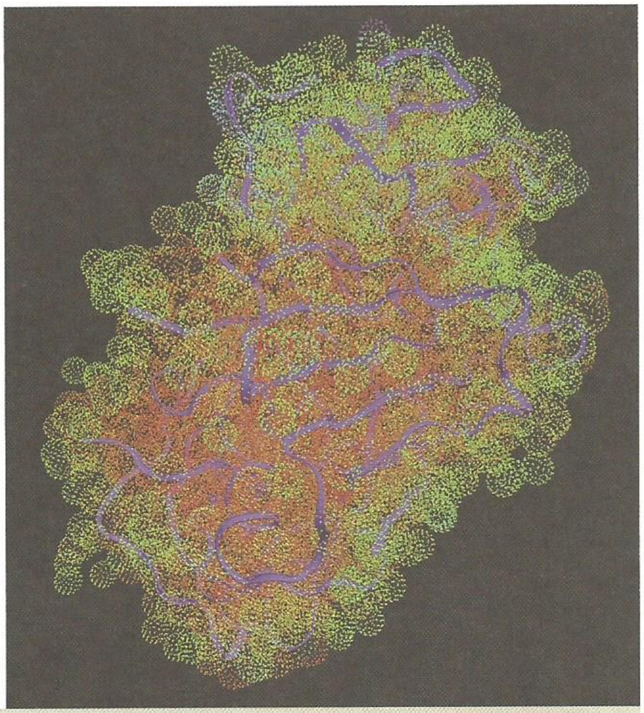
Through experiments carried out on birds and guinea pigs breathing in closed chambers and in a calorimeter (the latter experiment in collaboration with Pierre Simon de Laplace), Lavoisier identified respiration as a slow combustion in which carbon converts to carbonic acid and hydrogen to water, and heat and work are derived. To maintain its equilibrium, an animal or human must ingest in its food quantities of carbon and hydrogen equal to those consumed in respiration. Lavoisier could not specify in detail the nature of the substances containing the carbon and hydrogen, or the internal processes connecting the input to the final products of respiration, but his theory has provided ever since the boundaries within which the material exchanges between the organism and its surroundings and the dynamic chemical processes within the organism have been studied.

During the first four decades of the nineteenth century, the rapid development of chemistry provided increasingly powerful methods to study the composition of plant and animal matter and the transformations they undergo. By the 1830s, the three most important general classes of foodstuffs, as well as the major constituents of the organism, had been identified as carbohydrates, fats, and "albuminous" matter (later renamed proteins). The process of chemical change in the organism most open to direct investigation was digestion. A series of investigators, including Friedrich Tiedemann and Leopold Gmelin, Johann Eberle, Theodor Schwann, Louis Mialhe, Claude Bernard, and Willy Kühne, followed the changes that the three classes of foodstuff undergo in their passage through the stomach and intestines. In 1836, Schwann identified pepsin as a "ferment" that induced digestive changes in albuminous foodstuffs. The further characterization of pepsin has occupied investigators ever since. Pepsin became the prototype for the general concept that "ferments," acting in minute quantities as catalysts, direct many key processes in organisms. In 1876, Willy Kühne proposed the word "enzyme" to denote the class of ferments, including pepsin, that can "proceed without the presence of organisms." Later, his term gradually replaced the term ferment to denote the agents of both intracellular and intercellular chemical transformations.

During the 1840s, chemists and physiologists sometimes competed to determine the conditions under which the chemical processes of life could be established, chemists inferring their nature from the chemical properties of the substances involved, physiologists such as Claude Bernard insisting on the need to follow the chemical changes into the living body itself. Among the chemists, Justus Liebig and Jean-Baptiste Dumas showed how the new knowledge of the chemistry of proteins, carbohydrates, fats, and their decomposition products could be used to give more comprehensive meaning to Lavoisier's theory of respiration. Thus they took the first speculative steps toward an account of the intermediate stages connecting foodstuffs with final decomposition products and an ascription to these processes of the sources of animal heat and muscular work. Hermann von Helmholtz gave further meaning to these processes by linking them with his formulation of the general principle of the conservation of energy. Bernard demonstrated the fruitfulness of his approach by discovering through vivisection the special action of the pancreatic juice on fats and the glycogen function of the liver. Others saw the need to establish a new scientific specialty devoted to the study of the chemical processes of life. Carl Lehmann became a professor of physiological chemistry at Leipzig in 1847, and Felix Hoppe-Seyler professor of the same at Strasbourg in 1872. Both argued for the necessity of an independent discipline, but their example did not spread, and the subject continued to be pursued mainly in Institutes of Physiology in Germany, though a series of textbooks of physiological chemistry represented the subject as a coherent and growing body of knowledge and field of investigation.

During the second half of the nineteenth century, organic and physiological chemists identified a number of the amino acids obtainable by decomposing proteins. At the end of the century, Emil Fischer and Franz Hofmeister independently proposed that amino acids linked together through "peptide" (–CO–NH–) bonds compose proteins. Fischer also established the stereospecific formulas for a number of biologically important sugars. By this time it had become clear that starch, glycogen, and other "polysaccharides" were made of many simple sugars linked together. That fats can be decomposed into glycerol and fatty acids had been established early in the century by Michel Chevreul. The general appreciation that each of the three major foodstuffs could be broken down into smaller molecules, and growing evidence that this happened during digestion, led to the "building block" concept. This assigned the creation of proteins, fats, and carbohydrates of the organism to the reconstruction of similar materials, assimilated from the food, and transferred the central problem of "metabolism" from (in the words of Frederick Gowland Hopkins) "complex substances which elude ordinary chemical methods" to "simple substances undergoing comprehensible reactions." This shift in perspective energized the effort during the first decades of the twentieth century to detect the nature of the intermediary steps by new experimental methods. The discovery by Eduard Buchner in 1902 that the archetypical "ferment" (the agent of alcoholic fermentation) could be separated from yeast cells and produce "cell-free" fermentation further energized the search.

At the turn of the century, biochemical processes were studied in many institutional settings ranging from departments of physiology and organic chemistry to internal medi-



Computer graphic of the protein-digesting enzyme pepsin

cine, pathology, and brewery laboratories. In 1914, Hopkins acquired the title of Professor of Biochemistry, in a newly established Department of Biochemistry at Cambridge. Departments of biochemistry sprung up in the United States at leading medical schools, finding an institutional niche in the service role of teaching biochemistry to medical students. Although the discipline in Germany remained subordinate to physiology or organic chemistry, German scientists like Otto Warburg, Otto Meyerhof, Carl Neuberg, Franz Knoop, Heinrich Wieland, and Gustav Embden continued to dominate research in the field until the Nazi takeover in 1933 dispersed much of the German research community. Émigrés from Germany played a substantial role in the rise to prominence of biochemical research in American universities during the 1930s and the postwar period.

While some biochemists worked out metabolic pathways involving small molecules, others studied the structure of the largest biological molecules, the proteins. During the first two decades of the century, they ascribed special properties of proteins to their "colloidal state." After John Northrop crystallized pepsin in 1930, opinion shifted back to the view that proteins were large molecules of definite composition. Frederick Sanger established the complete sequence of amino acids in insulin between 1945 and 1955. But the earlier hope of finding larger patterns in the number and ordering of amino in proteins was not realized.

The crystallization of pepsin settled a long debate over whether enzymes were proteins or whether, as some prominent biochemists such as Richard Willstätter had maintained, proteins only acted as carriers for catalysts of small molecular weight. The study of the specificity and kinetics of enzyme reactions was one of the central focuses of biochemical research during the first half of the twentieth century.

In the 1920s, Warburg and Wieland proposed competing theories about the nature of biological oxidations. Warburg's theory that an iron-containing *Atmungsferment* transferred atmospheric oxygen to substrates undergoing oxidation seemed to be in conflict with Wieland's claim that cellular oxidations were dehydrogenation reactions catalyzed by "dehydrogenases." By the 1930s, these theories could be seen as complementary. Through this and associated research, a further class of smaller molecules essential to enzymatic oxidations and reductions, and named "coenzymes," was discovered.

By the mid-twentieth century, biochemistry appeared to be a flourishing, mature science dealing with a broad range of problems among the chemical phenomena of life. Rather suddenly, there arose a new discipline, named by its founders molecular biology, aimed at explaining biological phenomena at the molecular level. The new field crystallized particularly around the helical structure proposed in 1953 by James Watson and Francis Crick for the molecule of deoxyribonucleic acid, and the genetic implications inherent in it. Biochemistry and its predecessor fields had been involved with the investigation of vital phenomena at the level of molecules ever since chemical molecules had been defined in the early nineteenth century. Why then the need for a new field?

The answer is a mixed intellectual and social one. That the structure of DNA immediately offered a possible explanation of the molecular basis of the classical gene prompted a convergence between structural chemistry and genetics that had not been part of the agenda of biochemistry. Molecular biology hybridized two earlier fields. Also, some of the pioneers of the field of molecular biology, especially those who had moved into biological research from physics, had little training in biochemistry, regarded it as uninteresting, and hoped that they could solve the fundamental problems of life without it. Some biochemists, in turn, regarded newcomers to molecular problems as interlopers, and resisted their assimilation. The institutional separation that resulted has persisted, even though the barrier was artificial. Much of the investigation pursued in biochemical laboratories during the last decades of the twentieth century was indistinguishable from that carried out by molecular biologists, who have long since learned that they, too, need to incorporate biochemistry into their work and thought.

Frederic Lawrence Holmes

BIOLOGY. The word "biology," from Greek "life discourse," was introduced around 1800 by several authors to denote "the science of life" (Gottfried Reinhold Treviranus, 1802), or "everything that pertains to living bodies" (Jean-Baptiste Lamarck, 1802). The word conveyed the new, central role that the notions of life and organism were then acquiring, and a dissatisfaction with the emphasis on the mere classification of natural objects typical of naturalists of earlier generations. However, since Charles Darwin's *Origin of Species* could still do without the word "biology" in 1859, neither the word nor its introduction should be taken as rigid points of departure. Also, the Nobel Prize for "physiology or medicine," first awarded in 1901, did not and does not include the kind of natural history practiced by Darwin.

What we now call biology or the life sciences comprises a rich variety of research traditions and practices. They include, beside the general pursuit of knowledge, medicine, surgery, midwifery, pharmaceutics, agriculture, forestry, hunting, fishing, breeding, collecting, voyages of exploration, veterinary practice, food preservation and industries, biotechnology, and environment preservation. The places devoted to the study of the living world since the Renaissance also point to diversity. The medical school, university, anatomical theater, botanical garden, hospital, doctor's room, school of agriculture, veterinary school, natural history museum, field work, and the laboratory—each with its own set of goals, instruments, and habits—have all contributed to the shaping of what we now call biology.

The historical development of the life sciences fits the transition from natural knowledge to modern science set out in the article "History of Science," which derives primarily from the history of natural philosophy, but with some distinctive traits and contrasts. One such trait is that old research traditions seem to have coexisted with newer traditions more constantly and pervasively than in the physical sciences.

Because of these distinctive traits, the life sciences have received mixed reviews in appraisals of the Scientific Revolution, which until recently focused typically on the physical sciences. Because of these same distinctive traits, the history of biology offers scope for reflections aimed at resisting the recurrent temptation, on the part of scientists, historians, and philosophers alike, to force on science a simplified, unilinear pattern of historical development.

Thus, for example, the adoption of experimental techniques took on different forms in the life sciences depending on the field. Dissection—the main experimental technique revived in anatomy and medicine in the late sixteenth and early seventeenth centuries—stemmed mainly from within medicine itself, and implied no necessary revolt against the Aristotelian tradition, of the kind then frequent among astronomers and natural philosophers. The works of Andreas Vesalius on anatomy, William Harvey on the circulation of the blood, and Marcello Malpighi on development exemplify the shift toward experiment stemming from within the medical tradition.

During the seventeenth and eighteenth centuries, a growing number of new concepts and experimental techniques developed within natural philosophy and chemistry were introduced successfully into the life sciences. The works of René Descartes on physiology, John Mayow on respiration, Hermann Boerhaave on animal heat, Stephen Hales on perspiration, Albrecht von Haller on irritability, Lazzaro Spallanzani on generation, and Antoine-Laurent Lavoisier on respiration indicate how intense and creative the interaction between the life sciences and natural philosophy could be.

Meanwhile, much new information on the animate and inanimate objects of the globe—gathered through the voyages of exploration and the imperial networks set up by European powers from the fifteenth century onwards—was collected, named, and classified along lines suggested by the ancient natural history tradition revived by Renaissance humanists with their interest in erudition, antiquities, and collections. Largely unaffected by the mechanical philosophy of the seventeenth century, this tradition—cultivated by authors like Konrad Gesner, Ulisse Aldrovandi, John Ray, and Carl Linnaeus—continued to bear fruit well into the eighteenth century, especially in the fields of botany, zoology, systematics, the earth sciences, and paleontology.

Repeatedly in the early development of the life sciences, interests and practices that could be regarded as of merely specialist interest impinged upon broad philosophical and religious issues. For example, during the eighteenth century, in the controversy over generation, the concerns of naturalists and physicians merged and occasionally clashed with issues of interest to philosophers, theologians, and public authorities, producing a recurrent battleground for the ideological strands that characterized Enlightenment Europe. Enlightened curiosity and secularization made the egg, the animalcules supposed to be found in sperm, regenerating polyps, the microscopic animals found in vegetable and meat soups (called infusoria), monsters, fossils, as well as topics like the age of the earth, spontaneous generation, and extraterrestrial life subjects of enduring concern to philosophers and cultivated elites. Meanwhile, herborizing, entomology, and an amateur interest in natural history became fashionable among the leisured classes of European countries and their colonies. Similar interests continued to be popular well into the twentieth century and beyond, favored by the creation of natural history museums with their impressive dioramas and dinosaur displays, and by the entertainment and movie industries.

A combination of the traditional concerns and practices of the naturalist with philosophical, secularized theory-building is found also in the development of evolution theories and Darwinism throughout the nineteenth century. The history of evolution theories—a major component of the life sciences over the past two hundred years—reveals the extraordinary power that a blend of the empirical and the philosophical, the scientific and the popular, played in the history of biology. Here the works of Lamarck and Darwin, with their considerable impact on the general public, are emblematic.

A new experimental turn within the life sciences developed after 1839 with the introduction of cell theories and the new microscopic techniques used to explore the fine texture and development of living bodies. The works of Matthias Jakob Schleiden on plant cells and Theodor Schwann on animal cells promoted the idea that the cell was the fundamental unit of life, provided a powerful generalization for biology, and stimulated microscopical research. Together, they contributed to shaping the age of the (compound) microscope, a long, tremendously productive season in the history of laboratory biology and the medical sciences, which lasted until the introduction of the electron microscope in the 1930s.

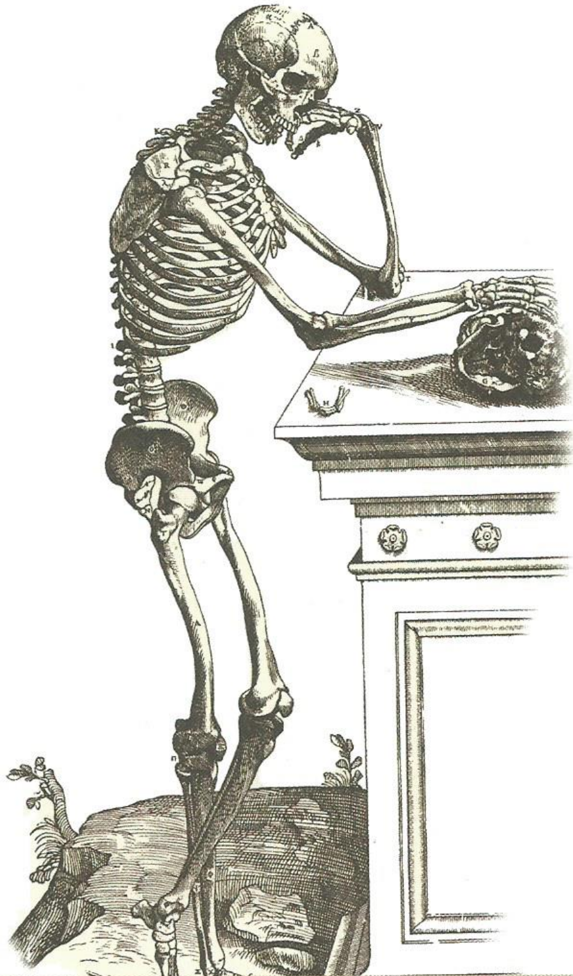
Early experimental developments in the life sciences were seldom accompanied by the sort of mathematization and quantification that the physical sciences underwent in the same period. Systematic, successful attempts at quantification first materialized in the central decades of the nineteenth century. These had their origins in the gradual affirmation of laboratory biology, the studies of Gregor Mendel on heredity, and biometrics.

The introduction of new instruments and the associated development of new laboratory techniques marked dramatic changes in the life sciences as in other fields of natural science. Chemical analysis and improved microscopes in the eighteenth and nineteenth centuries, X-ray crystallography and electrophoresis in the 1930s, the centrifuge and ultracentrifuge, chromatography and nuclear magnetic resonance from the middle decades of the twentieth century, the introduction of new monitoring techniques throughout the century, and the development of computational biology in the 1990s changed the outlook and perspectives of the life sciences repeatedly. The cumulative effect of these changes in laboratory technique, which had begun to accelerate with the earlier work of Justus Liebig, Claude Bernard, and Louis Pasteur, has been the enrollment of laboratory biology and medicine as major branches of the experimental sciences, and the growth of industries based on biological knowledge and techniques as new, powerful forces in society.

Despite this now recognizable trend, the panorama of the life sciences around 1900 still looked deeply fragmented. The unifying concepts offered by Darwin's theory of evolution in the 1860s and 1870s had only occasionally elicited the commitment of scientists working in other fields, like experimental physiology. The growing number of biologists trained in the laboratory and concentrating on such disciplines as cytology, embryology, or bacteriology felt uneasy about the controversy surrounding evolution theories. Biologists devoted to the empirical work of botany and zoology shared the malaise, while the continuation of Darwin's research tradition in the form of the biometric program developed by Francis Galton, Karl Pearson, and the adepts of eugenics often failed to appeal either to laboratory or field biologists.

The reemergence of Mendelian genetics in 1900, thanks to the works of Hugo de Vries, Karl Correns, and Erich Tschermak von Seysenegg, took place in this fragmented panorama, and for a quarter century seemed unable to contribute to its unification. Only after 1930 did some consensus on the mechanisms of evolution develop leading to the "evolutionary synthesis" or neo-Darwinian theory of evolution. Contemporary and later accounts of developments between 1920 and 1940 suggest, however, that the degree of unification achieved in biology through neo-Darwinism occurred via a federative effort rather than as a movement dominated by only one of the strands making up the field. Current historiography also testifies to the varied impact the synthesis produced in different disciplinary and national contexts.

Meanwhile, the consolidation of the research universities and the growing support given to the biomedical sciences by public and private bodies helped to launch powerful research schools that set new standards in training and research, and favored teamwork that occasionally transcended national borders. The work of Thomas Hunt Morgan and his school on the genetics of the fruit fly *Drosophila* during the 1910s and 1920s may be taken as prototypical. In the fly room—combining the old, simple tools of the naturalists and the sophisticated laboratory apparatus of the cytologists—biologists learned how to combine the laws of Mendelian genetics with laboratory work on the physical basis of the gene. A similar research school developed later in molecular genetics around the study of the viruses called *Bacteriophage*.



Articulated skeleton from *De humani corporis fabrica* (1543) by Andreas Vesalius (1514–64)

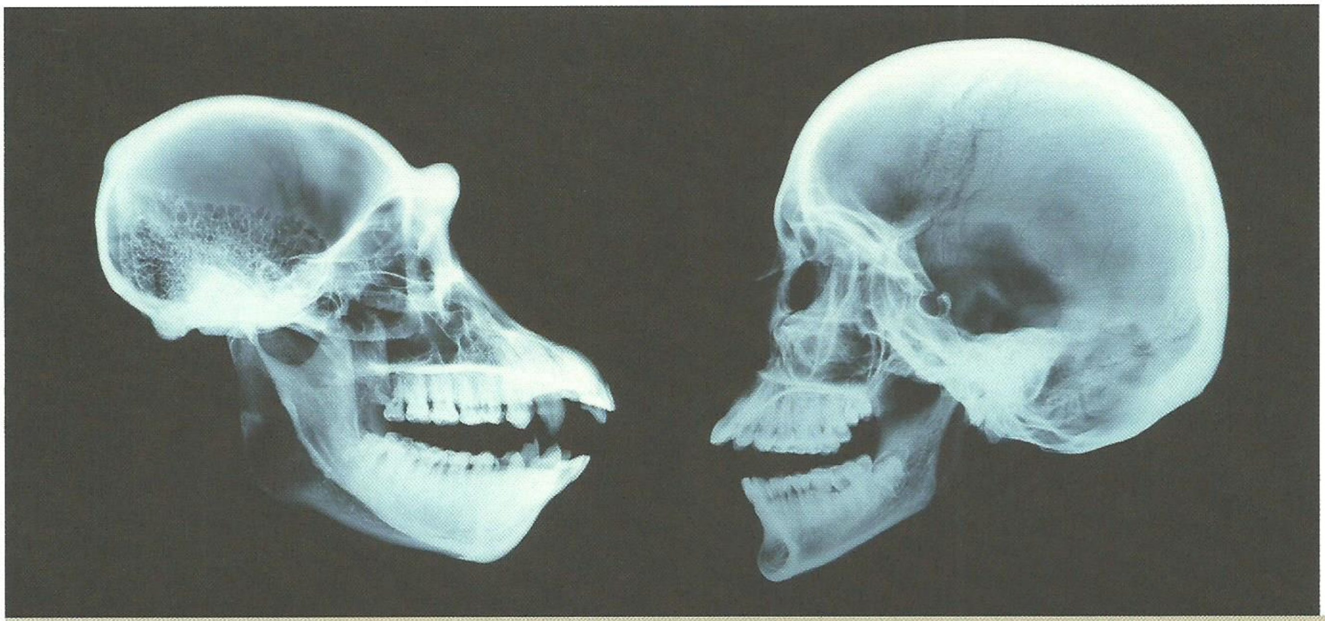
Meanwhile, evolution theories underwent important changes. Around 1930, R. A. Fisher, J. B. S. Haldane, and Sewall Wright developed mathematical methods that resulted in population genetics, demonstrating that a theory of natural selection could be based on (rather than, as some believed at the beginning of the twentieth century, refuted by) Mendelian genetics. Population genetics also showed that statistics and mathematical modeling could be basic tools for evolutionary biologists, as they were for physicists.

From the 1940s onwards, two other fronts potentially controversial for evolution theories—systematics and paleontology—fell into line in the works of Theodosius Dobzhansky, George Gaylord Simpson, Ernst Mayr, and their pupils. The evolutionary synthesis could be presented as proof that biology had at last some unification and a widespread consensus around the heritage left by Charles Darwin. Biologists and historians of biology thus represented the synthesis during the centennial celebrations in 1982 commemorating Darwin's death.

The neo-Darwinian synthesis had (and retains) several features appealing to the era of the cold war, when expert and lay audiences alike looking for broad generalizations thought to answer the challenges, and tame the uncertainties, associated with the deep ideological commitments and recurrent conflicts of a divided world order. However, in the early 1980s, just when the synthesis was being celebrated as the major development of twentieth-century biology, it was losing its central position in the life sciences. It no longer reflected the increasingly experimental and instrumentalist ethos attracting biologists and their public.

Since the early 1950s, molecular biology had been shifting the careful balance pursued within the synthesis between the naturalists' and the experimenters' traditions of the life sciences in favor of the experimenters. The shift had been prepared during the 1930s by incursions of leading physicists like Niels Bohr into the terrain of biology, followed by the pathbreaking work of biologists with a background in physics like Max Delbrück, and by books such as Erwin Schrödinger's *What Is Life?* (1942). The new shift of biology toward experiment, the laboratory, and the techniques and metaphors of the new information technologies born of World War II, was later celebrated by biologists in books addressed to a wide public, like James Watson's *The Double Helix* (1968), Jacques Monod's *Chance and Necessity* (1970), and François Jacob's *The Logic of Life* (1970).

The identification of DNA as the carrier of heredity in the 1940s, the discovery of the double-helix structure of DNA by Francis Crick and James Watson in 1953, the breaking of the genetic code in the mid-1960s, and the development of recombinant DNA techniques leading to the emergence of biotechnology industries in the 1970s all can be depicted as the products of a new wave of instrumentalism in biology. So can initiatives like the publicly funded, international Human Genome Project, launched in 1988, and the publication in 2001 of two draft sequences of the human genome produced by biologists participating in the project and by the firm Celera Genomics. Instrumentalism fueled by computer-based techniques and inspired by the conceptual tools of the information sciences seems to constitute the main



X-ray photographs of chimpanzee and human skulls. The chimp has a bigger jaw bone, the human more brain capacity

connecting thread among these developments, though perhaps not the compass likely to orient biologists toward the long-sought unity of the life sciences.

The detailed recent histories of the people, research schools, laboratory techniques, national institutions, foundations, private industries, and transnational groups of scholars involved in the development of the biomedical sciences during the second half of the twentieth century indicate a complex story. The wealth of stimuli generated by the diverse interests, training, disciplinary traditions, and cultural backgrounds of a growing international population of researchers seems no less important than the overall instrumentalist strategy adopted by the leading actors and programs. A portrait of the life sciences at the turn of the twenty-first century would emphasize the tensions as well as the synergisms among the major, different threads that continue to make up biology. Given the rapid emergence and disappearance of specialties, fields, and subfields, the major threads can best be identified through a few catchwords used by experts, science policy-makers, science journalists, and the public when trying to capture the current focus of biology: "life sciences," suggesting the multiplicity of research traditions and practices that continue to be deployed by humans in order to understand and bend to their own advantage life and its complexity; "evolution," referring to the persistent expectation, associated with the life sciences generally and anthropology in particular, that biology can tell us something about our place in nature; "neurosciences," alluding to the widespread feeling that the brain is the next citadel to be addressed; and "biotechnologies" and "bioethics," currently the most popular of the catchwords, as indicating the powerful, manipulative skills through which biologists have at last joined other scientists and technologists in supplying high-tech goods for the planetary market economy of the turn of the century, and as evoking the mixture of expectations and fears that their new power is generating in the public.

GIULIANO PANCALDI

BIOMETRICS, or biometry, is the statistical study of populations of living organisms and their variations. Biometrics had its origin in the collaboration between W. F. R. Weldon and Karl Pearson at University College London (UCL) from 1891 to 1906. As a morphologist, Weldon was interested in the functional relationships between the physical characteristics of living organisms. But Darwin's theory of evolution by natural selection had changed the context in which morphologists thought about those relationships. His theory challenged future generations of researchers to answer two fundamental questions: how were physical characteristics passed on to offspring, and could the process of natural selection cause the physical character of a population to deviate enough to make it a new and separate species? Investigating the latter question, Weldon realized that before a determination whether natural selection could cause significant deviation in the physical character of a population could be made, ways for measuring the influence of heredity and for establishing the normal degree of variation for a given species had to be established. Weldon concluded, therefore, that the question of the efficacy of natural selection was a statistical question. To make the necessary measurements and calculations, he borrowed the concepts and techniques of correlation and regression developed by Francis Galton in his *Natural Inheritance* (1889). Soon, however, Weldon confronted his own inadequacies as a statistician and turned to Pearson.

Pearson, a Cambridge-educated mathematician, was a polymathic dabbler. Living in London in the 1880s, he made his mark as a freethinking socialist and as an advocate of scientific rationalism. Appointed to the chair of applied mathematics and mechanics at University College in 1884, Pearson found a focus for his mathematical work once he began to collaborate with Weldon, who came to UCL in 1891 as the new Jodrell Professor of zoology.

Pearson also had been impressed with Galton's *Natural Inheritance,* both for its statistical approach and for its eugenic concerns. Under Weldon's influence, Pearson began work on ways to adapt and extend the concepts of correlation and regression to statistical problems presented by the study of dynamic populations. The work done by Pearson between 1891 and 1896 laid many of the foundations of modern statistical theory. By 1900, researchers who applied statistical theory to the study of populations of living organisms were identified as the "biometric school."

The school faced severe criticism of its methods from researchers who, bolstered by the "rediscovery" of Gregor

Mendel's theory of heredity, argued that the study of genetics held the key to understanding evolution. Faced with this challenge, Pearson and Weldon launched *Biometrika* (1901), a journal dedicated to "the statistical study of biological problems." The controversy between the biometricians and the Mendelians raged for more than two decades.

Biometrics continued to be controversial, both for its statistical approach and for its ties to eugenics, until the 1930s, when the final elements of a synthesis of biometrics and Mendelism were put in place. One of the contributors to the synthesis, R. A. Fisher, another Cambridge-trained mathematician, succeeded Pearson in 1933 as Galton Professor of eugenics at UCL. Fisher became interested in evolution by reading Pearson's articles entitled "Mathematical Contributions to the Theory of Evolution." Fisher sought to demonstrate the compatibility between the effects of Darwinian natural selection as described by biometrics and Mendelian genetics. His paper of 1918, "The Correlation Between Relatives on the Supposition of Mendelian Inheritance," did much to establish that compatibility. By the late 1930s, work in a similar vein by Sewall Wright and J. B. S. Haldane had completed the synthesis and laid the foundations for the science of population genetics.

Meanwhile, Pearson's successor as editor of *Biometrika,* his son, Egon Pearson, took advantage of the cessation of hostilities between the biometric and Mendelism camps. No longer needing to defend the legitimacy of the statistical study of evolution, he began to purge *Biometrika* of its antigenetics rhetoric and of its eugenic concerns, transforming biometrics into the production of statistical tools and data for use by biologists of all persuasions.

JEFFREY C. BRAUTIGAM

BIOTECHNOLOGY. The Hungarian scientist Karl Erky coined the term "biotechnology" in the title of a treatise that he published in 1919 calling for an industrialized agriculture for the production of meat, fat, and milk. Erky's program built on processes that involved fermentation to produce goods like beer. The growing understanding that microbiological processes are chemical ones turned Erky's branch of biotechnology toward the exploitation of biological organisms to work on an industrial scale. After World War II industrial biotechnology expanded into the production of pharmaceuticals such as penicillin and, in the 1960s and 1970s, into attempts to coax single-cell organisms to transform hydrocarbons into edible proteins and barnyard waste into gasohol. Japan, Germany, Britain, and the European Commission encouraged these programs because they promised to yield better medicine and more abundant food and materials, and to bolster international competitiveness in the face of declines in traditional manufacturing.

A new biotechnology, which depended on molecular genetics, particularly the technique of recombinant DNA, was invented in 1973 by Stanley Cohen, at Stanford University, and Herbert Boyer, at the University of California San Francisco Medical School. Their technique allowed biologists to snip out a gene from the genome of one species and insert it into the genome of another, where it might replicate and express itself. The method was first used to insert foreign genes into bacteria to study their function, but molecular biologists recognized that it could be employed to modify virtually any organism, including plants, animals, and perhaps even human beings.

To many scientists, the fact that humans could now easily create combinations of genetic material unknown in nature was more worrisome than welcome. They feared that, while many DNA hybrids would no doubt prove to be innocuous, some—for example, bacteria containing genes suspected to cause cancer—might be hazardous to human health. In response to that fear, 140 biologists from the United States and Europe convened in February 1975 at the Asilomar Conference Center, on the Monterey Peninsula, in Pacific Grove, California, to probe the promise and hazards of joining DNA across species. The conference agreed that recombinant research could and should be done under guidelines that ensured its safety. Variants of the guidelines were adopted by the National Institutes of Health in the United States and its counterpart research agencies in Europe.

From the mid-1970s onward, recombinant research proceeded with increasing momentum, spurred ahead not only by its scientific but also its commercial possibilities. Molecular biologists predicted that it would revolutionize medicine, by replacing disease-causing genes with normal ones; pharmaceuticals, by turning bacteria into factories for the production of drugs to order; and agriculture, by equipping plants to fix their own nitrogen from the air.

Some of the biologists, including Herbert Boyer, took their case to investment bankers. Together with a young venture capitalist, Boyer scraped up $1,000 to found a biotechnology company to exploit recombinant DNA commercially. The company was formally incorporated (with additional capital including $100,000 from Thomas Perkins of the Kleiner and Perkins firm) as Genentech ("genetic engineering technology").

Boyer and Swanson determined that Genentech's first project should be the production by recombinant techniques of human insulin. The world's supply of therapeutic insulin came from the pancreases of slaughtered cows and pigs. Projections at Eli Lilly & Co., which accounted for at least 80 percent of all insulin sales in the United States, indicated that the insulin needs of the American diabetic population might eventually outrun the animal supply. In early September 1978, at a crowded press conference, Genentech announced that it had bio-engineered human insulin and that, about two weeks earlier, it had entered into an agreement whereby Eli Lilly & Co. would manufacture and market the hormone. When in mid-October 1980, Genentech—assigned the stock symbol "GENE"—went public, investors snapped up its shares at more than twice the offering price of $35, astonishing Wall Street observers.

The financial markets' strong interest in biotechnology was matched by the attention it now received among federal policymakers in the United States. Biotechnological products promised to increase the country's international trade surplus in high-technology goods, which since the mid-1970s had been offsetting a sizable trade deficit in other types of manufactures. In 1980, the government granted the biotechnology industry a triple boost: the National Institutes of Health virtually ended its restrictions on recombinant research; Congress passed the Bayh-Dole Act, which explicitly encouraged universities to patent and privatize the results of federally sponsored high-technology research; and in June, the United States Supreme Court ruled in *Diamond v. Chakrabarty* that a patent could be issued on a genetically modified living organism, holding, over the legal and moral objections of critics, that whether an invention was living or dead was irrelevant to its qualification for intellectual-property protection.

Building on the Chakrabarty case, the United States Patent Office issued its first patent on a genetically engineered plant in 1985 and the first patent on an animal in the history of the world in 1988 (a mouse genetically modified at Harvard to be supersusceptible to cancer). Biotechnology soon received similar encouragement from the European Community. In 1991, the European Patent Office granted Harvard a patent on its mouse, and in 1998 the European Commission, the executive arm of the Community, issued a sweeping directive authorizing patents on a wide range of biotechnological inventions.

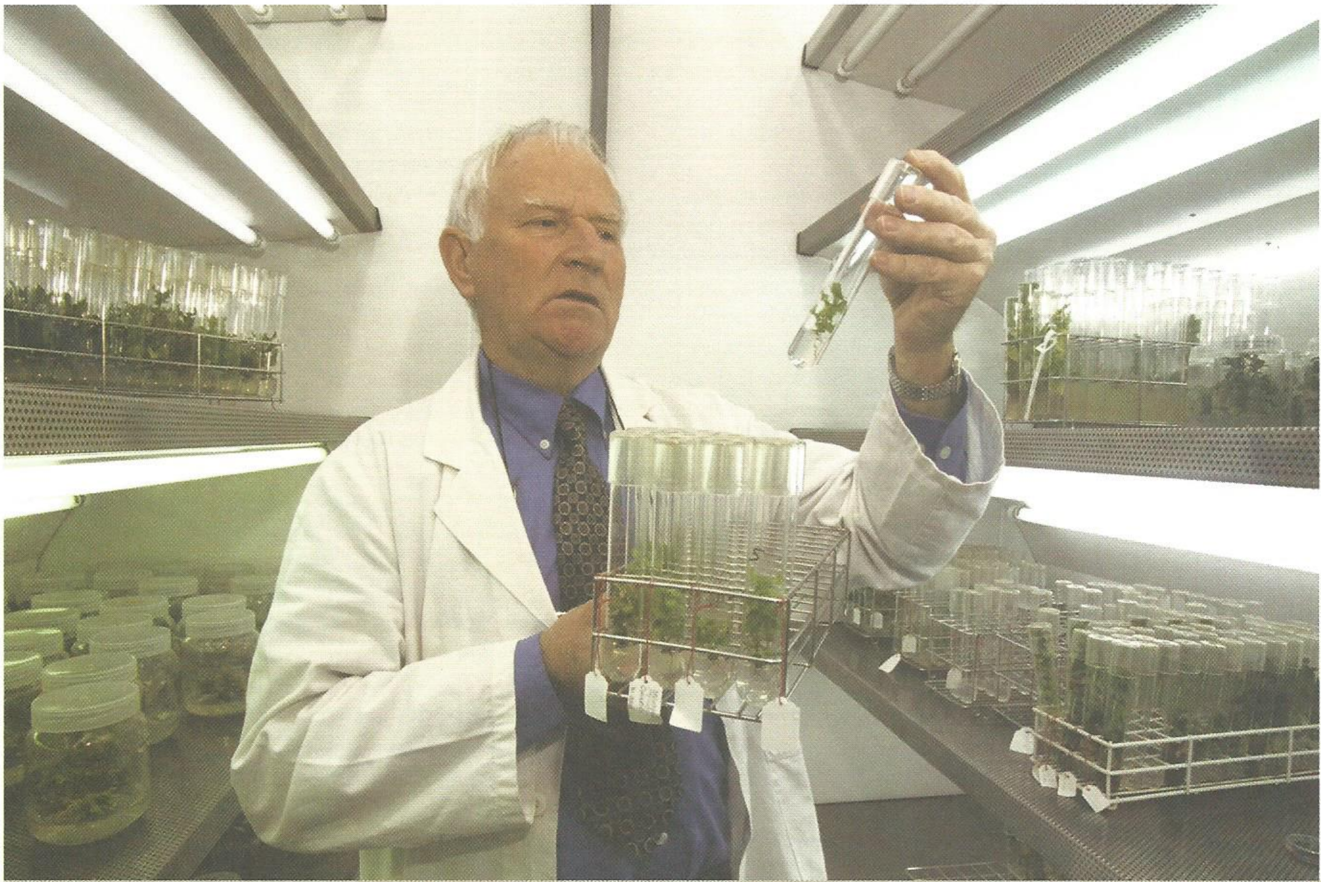
By the 1990s, the biotechnology industry had established itself in the United States and Europe and had branches in Asia and Latin America. In 1999, it generated $20 billion in revenues in the United States alone. It comprised start-up firms, many of them spun off from academic laboratories, as well as major pharmaceutical companies and several oil and chemical giants that supported research programs of their own or purchased one or more of the fledglings. Some 80 to 90 percent of the biotechnology companies produced pharmaceuticals and health-service tests.

Agricultural biotechnology accounted for about 10 percent of the industry with plants engineered to resist pests and pesticides or to remain fresh longer after harvest. Some firms in the agricultural area attempted to modify animals genetically with the goal of making sheep that produced more and better wool or cows and pigs that provided more and leaner meat. A few pioneers in "molecular farming" tried to turn common animals genetically into factories for the production of valuable human proteins otherwise difficult and expensive to obtain, if they could be obtained at all.

Yet the new biotechnology had been creating enemies since its inception. Scientists and laypeople both questioned the wisdom of leaping into research with recombinant DNA, holding that the resulting organisms might threaten delicate ecological balances and that, in any case, creating them would be an act of hubris, an assumption of the powers of God. As the biotechnology industry developed, the attention of the critics turned to the patenting of living organisms, the best purchase they could obtain on the advancing biotechnological juggernaut. Some critics declared that such patents would foster monopoly in vital areas such as the food industry; others insisted that the genetic engineering of animals would lead to their suffering; still others contended that patenting them was sacrilegious, turning God's creatures into commodities. In the 1990s, when the Human Genome Project fostered the rapid identification and patenting of genes, one dissident warned the United States Congress that "we are right in the middle of an ethical struggle on the ownership of the gene pool."

The critics made no significant headway until the late 1990s, when genetically modified foods began coming to market. In the United States, these foods, those derived from corn, soy, canola, cotton, and milk, were too widespread to avoid easily. They were also making inroads abroad. Europeans greeted their arrival with protests and boycotts. Critics called them "Frankenfoods" and claimed that they posed hazards to human health because they contained proteins that did not occur in the natural varieties of food crops. The outcry spread to the United States and led a number of food markets to refuse to stock genetically modified products.

Most of the genetically modified food crops available in 2000 had been designed to assist agricultural producers. A notable example, the Monsanto Corporation's Round-Up Ready soybean, was engineered to withstand the company's Round-Up pesticide. Analysts suggested that once the agricultural biotechnology industry produced foods directly



A scientist cultures Chinese artichokes at ENITHP (Ecole Nationale d' Ingenieurs des Travaux de l' Horticulture et du Paysage d' Angers) as part of a project to preserve and improve traditional crops.

beneficial to consumers, the opposition would diminish. But whatever the future may bring to agricultural biotechnology, the biomedical sector of the industry continues to flourish and enjoy the strong support of the public, including investors, because of its promise for health care.

D. J. Kevles

BLACK HOLE. A black hole in space has a gravitational force so strong that nothing can escape from it, not even light. Hence no one can see a black hole, but astronomers are convinced they exist. An early intellectual precursor to the concept of black holes may be found in John Michell's dark stars. Michell noted in 1783 that if bodies with densities not less than the Sun's, and hundreds of times greater in diameter, really existed, gravity would prevent their light particles from reaching us. Their existence might be inferred from the motions of luminous bodies around them. Michell's idea was ignored even before wave theory, in which gravity does not act on light, overthrew the particle theory from which he reasoned.

Collapsed stars make another intellectual precursor to black holes. After 1915 and Einstein's relativity theory, gravity again could act on light. In the 1930s, Subrahmanyan Chandrasekhar, recently arrived from India to study in England, modeled stellar structures. He found that stars of less than 1.4 solar mass shrink until they become white dwarfs, but more massive stars continue contracting. The British astrophysicist Arthur Eddington noted that at high compression, gravity would be so great that radiation could not escape, a situation he regarded as absurd. Others accepted Chandrasekhar's mathematics but believed that continuous or catastrophic mass ejection would act as a universal regulating mechanism to bring stars below the critical mass. Also, massive stars might evolve into stars composed of neutrons. In 1939, however, the American physicist J. Robert Oppenheimer established a mass limit for neutron stars. When it has exhausted thermonuclear sources of energy, a sufficiently heavy star will collapse indefinitely, unless it can reduce its mass.

World War II and then the hydrogen bomb project diverted research away from stellar structure. Nuclear weapons programs, though, did develop a deeper understanding of physics and more powerful computational techniques, and in the 1960s, computer programs that simulated bomb explosions were modified to simulate implosions of stars. A renewed theoretical assault followed on "black holes" as they were named by the American nuclear physicist John Wheeler in 1967. In contrast to collapsed or frozen stars, black holes are now known to be dynamic, evolving, energy-storing, and energy-releasing objects.

Because no light escapes from black holes, detection of them requires observing manifestations of their gravitational attraction. From a companion star, a black hole captures and heats gas to millions of degrees, hot enough to emit X rays. Because the Earth's atmosphere absorbs X rays, devices to detect them must be lofted on rockets or satellites. A few black holes probably have been found, although other explanations of the observational data are possible.

In another predicted manifestation, two black holes spiral together, gyrate wildly while coalescing, and then become steady. Outward ripples of curvature of spacetime, also called gravitational waves, would carry an unequivocal black-hole signature. Gravitational waves should propagate through matter, diminishing in intensity with distance. On Earth, they should create tides the size of an atom's nucleus, in contrast to lunar tides of about a meter. Gravitational-wave detectors may be operational early in the twenty-first century.

Meanwhile, without benefit of prediction and intent, we may already have observed manifestations of black holes. Extraordinarily strong radio emissions from both the centers of galaxies and from quasars (compact, highly luminous objects) maybe powered by the rotational energy of gigantic black holes, either coalesced from many stars or from the implosion of a single supermassive rotating star a hundred million times heavier than our sun. Other possible explanations for radio galaxies and quasars, however, do not require black holes.

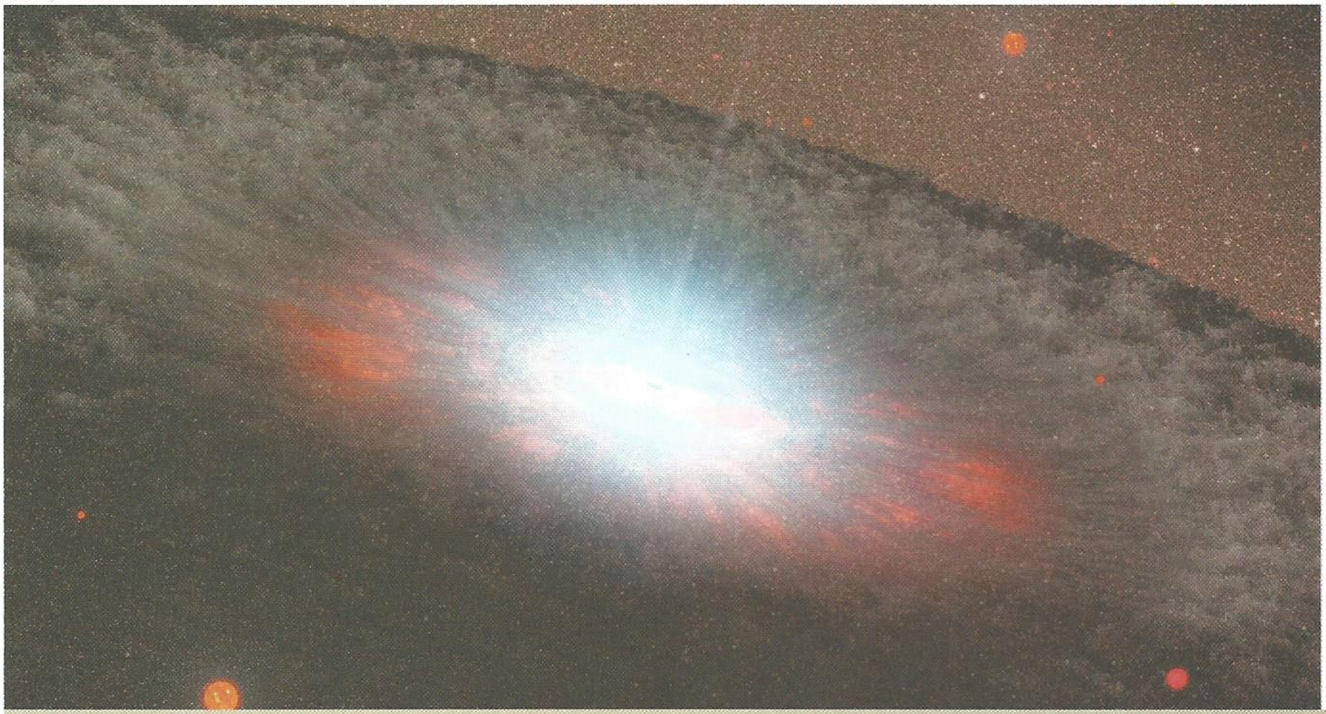
Norriss S. Hetherington

BLOOD is a complex physiological fluid essential to a wide array of life-supporting functions in the body. Through the circulatory system of arteries, veins, and capillaries, blood transports oxygen from the lungs to cells, and removes waste products like carbon dioxide and other cellular metabolic by-products, delivering them to the lungs, kidneys, and skin for excretion. In addition, blood is the primary vehicle of immunity. White blood cells, or leukocytes, constitute the cellular components of the immune system, responsible for warding off infections and infiltration of foreign proteins.

Since antiquity, blood has been regarded as integral to life. Recognizing that the heart and blood vessels were connected in a unified system, Aristotle defined the blood as a nutritive fluid that sustained the vitality of the solid parts of the body. In the Hippocratic and Galenic traditions, blood was identified as one of the four humors that comprised the human body. In this tradition, health and disease were interpreted as the result of the interaction of these four constituents. Imbalance or disequilibrium in the humors offered a powerful rationale for bloodletting or phlebotomy, which remained an important medical therapy for more than two millennia.

Initial interest in the blood focused on its physical movement in the animal and human body. In the early seventeenth century, English physician William Harvey provided statistical and experimental support in *De Motu Cordis* (1628) for his claims that blood circulated in the bodies of animals and humans. At this time, physicians made little differentiation between the blood of animals and humans, as the earliest efforts in transfusion illustrate. In 1667 French physician Jean Baptiste Denis performed the first human transfusion when he transfused blood from sheep and calves into several patients. At the Royal Society in London, English physician Richard Lower paid a clergyman the sum of one guinea for his willingness to "suffer the experiment of transfusion" with blood from a lamb.

The advent of the microscope revealed that blood was not a simple, uniform fluid. The Dutch lens maker Antoni van Leeuwenhoek, examining his own blood under a primitive microscope, first identified the red blood cells, the small, red globules "swimming in a liquor, called by physicians, the serum." Jan Swammerdam and Marcello Malpighi, who identified the role of the capillaries in the circulatory system, also noted these corpuscles. English physician William Hewson was among the first to describe white blood cells, or leukocytes, and demonstrated some of the essential features of blood clotting or coagulation. In 1851 German physiologist Otto Funke identified hemoglobin, the reddish pigment in red blood cells. Investigations by Felix Hoppe-Seyler established that hemoglobin was responsible for taking up and discharging oxygen. Using new chemical dyes and improved microscopes, Paul Ehrlich profoundly influ-



Black hole at the center of a galaxy, an artist's conception based on data collected by NASA's Galaxy Evolution Explorer. Radiation (blue) is so intense it drives matter away; the gray material is a ring of gas.

enced the development of hematology. Ehrlich identified several new types of white blood cells, described differences between healthy and diseased blood cells, and distinguished the various forms of anemias.

In the early twentieth century, attention focused on the role of blood in the immune system. In 1900, Karl Landsteiner discovered that human blood could be divided into three groups when he combined red blood cells of individuals with the sera taken from others. (The fourth, rarer blood group was identified by two of his associates, who tested a larger group of people.) Although surgeons attached little importance to this work before World War I, the importance of blood grouping to avert transfusion reactions intensified when Landsteiner, with Alexander Wiener, discovered in 1940 the Rh blood group, a major cause of fetal and infant death. In the 1950s, serologists sought to define the antigens on white blood cells. In 1958, Jean-Baptiste Dausset reported his discovery of a gene complex (human leukocyte A complex) that accounted for different immunological responses in blood transfusions. The identification of other human leukocyte antigens (HLA) followed; these formed the basis of the HLA system for typing tissues and organs to reduce the threat of organ and tissue graft rejection in transplantation.

During World War II, the biochemist Edwin Cohn pioneered a new method for plasma fractionation of human blood, fostering renewed interest in blood biochemistry. Cohn's method for separating the protein fraction from plasma and the production of such pharmaceutical products as gamma globulin (used in the treatment of infectious disease) and antihemophilic factor (which altered the lives of thousands of hemophilia patients) ushered in a new era of blood-based research. Extending some of the work on blood fractionation, chemist Linus Pauling studied the physical chemistry of hemoglobin variants and their role in sickle cell disease. In 1949, Pauling concluded that the inherited disorder resulted from a flaw in the molecular composition of hemoglobin, and proclaimed sickle cell anemia to be the first molecular disease. Although significant for the emergence of molecular medicine, these insights did not foster immediate clinical benefits for sickle cell patients.

Over the course of the twentieth century, the therapeutic advances in blood transfusion and blood components provided an important and life-saving medical intervention. At the same time, the therapeutic use of blood fostered new dangers; medically administered blood became the vehicle for the transmission of disease. During World War II, the infection of military personnel with hepatitis raised serious concerns that disease might spread through the blood supply. In the 1980s, blood-borne spread of a hitherto unknown virus, the human immunodeficiency virus (HIV), was linked to a newly identified and lethal disease, AIDS. Although heat treatment and viral antibody testing have decreased the threat of HIV transmission, concern about the transmission of such diseases as Mad Cow Disease continue to trouble blood bankers and health policy makers.

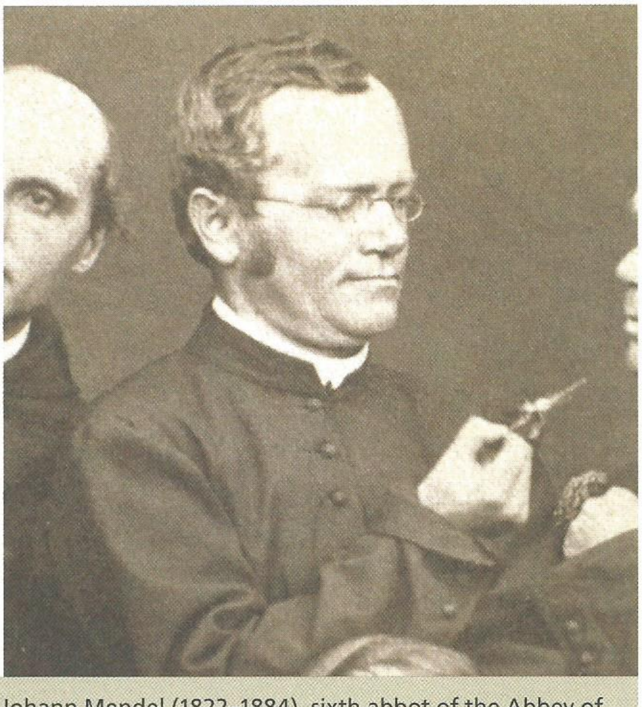
Blood is a potent biological substance studied by physicians and medical researchers; blood is also a complex cultural entity with social meanings that vary considerably with time and place. Ideas about blood purity extend far beyond the physical properties of a biological fluid to encompass notions about social networks and contamination—both moral and physical. In twentieth-century Japan, many believed that a person's blood type determines personality and character. In the American eugenics movement, blood and heredity were often closely linked in ideas about lineage or bloodlines. As Karl Landsteiner had predicted, the science of blood came to play an important role in forensic science and in cases of disputed paternity. By the 1930s, German, Austrian, and Danish courts all accepted blood tests for establishing paternity. In the United States, courts remained reluctant for decades to rely on serological tests to establish paternity, and, in the case of several highly publicized cases in which infants were mistakenly given to the wrong parents, maternity. Serological tests to determine guilt and innocence in criminal proceedings came to play an important role in criminal prosecutions on both sides of the

Atlantic. Even as DNA testing has come to dominate such proceedings, blood remains a powerful signifier.

Susan E. Lederer

BOTANY. Much of the earliest botany was concerned with *materia medica*. An exception, the work of the ancient Greek philosopher Theophrastus, classified plants in the Aristotelian tradition. He included much information on the agricultural techniques of his day. But by far the most famous ancient text was Dioscorides's herbal, a plant encyclopedia written in Greek for physicians. Translated subsequently into Latin and Arabic, and copied and recopied, often with additions and manuscript illustrations because herbalists and apothecaries had to be sure of the plants' identities, Discorides's work underwrote the first printed herbals, particularly those of Otto Brunfels and Leonhart Fuchs. These were expensive books, often hand-colored and annotated, which circulated mainly among physicians, theologians, university dons, and courts.

During the late sixteenth century practitioners increasingly noticed that Arabic or ancient texts did not describe the plants of western Europe and started adding to traditional lists. This enlargement coincided with the colonial expansion of Europe, most notably into the East Indies and the New World, and changing systems of medical education, itself partly a consequence of the new texts available. Plants, remedies, and herbs were introduced to Europe from overseas, encouraging the development of the physic gardens already attached to the main universities, enriching the gardens of the royal courts, and posing questions about geographical distribution. By the end of the century, Rembert Dodoens and William Turner were producing works not so much to supplement but to replace ancient ones. Herbals and botanical compendia continued to be published in large numbers in relatively stereotyped format. Nicholas Culpeper's *English Physician Enlarged; or. The Herbal* (1653) was typical. Through these volumes, countless people learned a utilitarian and domestic combination of medical and botanical science.



Georg Johann Mendel (1822–1884), sixth abbot of the Abbey of Saint Thomas in Brno, Czech Republic, and a founder of genetics

During the seventeenth century, the study of botany broadened to come into contact with other disciplines besides medicine and classification. The use of the microscope in Britain, Italy, and the Netherlands revealed the unsuspected world of the small. Robert Hooke saw "pores" in cork, which he called "cells." Nehemiah Grew and Marcello Malpighi independently identified the principal tissues of the plant body, including stem, root, and leaf. Plant functions were mostly interpreted by analogy with animals. For Grew the xylem vessels resembled animal tracheae; Stephen Hales suggested that plant sap circulated like blood. Grew also identified stamens as the male reproductive organs and supposed that plants possessed two sexes, again like animals. Proof came in the work of Rudolph Jakob Camerarius in 1694, although the sexuality of plants was contested for decades afterwards.

The Swedish doctor Carl Linnaeus transformed botany in the eighteenth century by devising an "artificial" classification system whereby plants were sorted into higher taxa by the numbers of stamens and pistils they possessed. Linnaeus trained and sent plant collectors all over the increasingly accessible globe, to Japan, South Africa, the Carolinas, Asia, and central Spain. They found many specimens of plants unknown in Europe. Linnaeus also set out philosophical principles for the science. He introduced binomial names, the first denoting the genus, the second the specific character of an individual. Furthermore, Linnaeus helped botanical knowledge move out of the elite sphere of universities, museums, and physic gardens to a broader constituency. Many gentlefolk, women, and working men encountered botany through popularizations of Linnaeus's writings. His devout definition of plant species as stable entities, fixed since their creation by God, stimulated studies of hybridization, which even Linnaeus conceded must occur sometimes. Johann Wolfgang von Goethe proposed that all floral parts had been modified from leaves. Later, Augustin-Pyramus de Candolle formulated useful concepts of symmetry, abortion, modification, and fusion.

During the nineteenth century naturalists turned to the functional anatomy of plants. Robert Brown made important investigations into fertilization before making his better known discoveries of the cell nucleus and Brownian motion. Jacob Mathias Schleiden laid the groundwork for the cell theory of Theodor Schwann. Hugo von Mohl summarized advances in cell anatomy in 1851. Meanwhile fundamental observations, including identification of free swimming spermatozoids, were made on the nature of fertilization in algae. René-Joachim-Henri Dutrochet studied osmosis. J. B. J. D. Boussingault elucidated the nitrogen cycle. The essential steps in carbon fixation were recognized when Julius von Sachs showed that the starch present in green cells came from the carbon dioxide absorbed. Gregor Mendel and Charles Naudin did essential experimental work on plant hybridization. Modern perceptions of the overwhelming importance of evolutionary theory have obscured the significance of these physiological, experimental, and microscopic investigations.

Although evolutionary theory gave the geography and morphology of plants new legitimacy, physiology led the way. Sachs's *Lehrbuch der Botanik* (1868) inspired every plant physiologist with the hope of spending time in Sachs's laboratory in Wurzburg. Sachs made significant studies on plant hormones, growth mechanisms, and tropisms like the effect of gravity or light on roots and shoots. The emphasis of research shifted so much toward the physiological, notably in enzyme studies and fermentation, that Joseph Dalton Hooker in Kew

Gardens, England, felt it necessary to reassert the value of taxonomy as an academic discipline in the *Index Kewensis* and his and George Bentham's *Genera Plantarum*. Botany soon became the prime area for genetic research, as in pure-line experiments, cytology, fertilization, and cell division.

In the twentieth century increasing investigations into fossil plants led to debate over the origin of flowering plants (angiosperms) in the Cretaceous period. This also involved controversy over what should properly be considered primitive. Plant paleontology became an important part of science with the rise of quarternary studies, the study of the geology and environment of the recent archaeological past.

JANET BROWNE

BUREAUS OF STANDARDS. The origin of national and international bureaus of standards lies in the interest in metrology during the late eighteenth and early nineteenth centuries. On the eve of the French Revolution, France had over a thousand legal units of measurement with approximately 250,000 local variations. Spurred on by the work of French and foreign natural philosophers, the French government began to revamp its metrological system. French experimental natural philosophers argued that all of the earlier systems of the ancien régime needed to be disposed of, and a new standard based on precision and simplicity needed to be implemented. In 1790 the French Academy approved the decimal metric system. On 22 June 1799 platinum standards of the meter and the kilogram were placed in the Archives in la République de Paris. The leading German physicist and mathematician of the early nineteenth century, Carl Friedrich Gauss, promoted the kilogram and meter, as well as the second, as the units of the physical sciences. His measurements of the earth's magnetic force pioneered the use of these three units and their derivatives. Subsequent research by Gauss and Wilhelm Weber on electrical phenomena also employed this set of units.

James Clerk Maxwell and Joseph John Thomson furthered Gauss and Weber's research under the aegis of the British Association for the Advancement of Science (BAAS). In 1874 the BAAS announced the CGS system, a unit system based on the mechanical units of the centimeter, gram, and second and adding a set of standardized prefixes, from micro to mega, indicating levels of magnitude. During the 1880s, the BAAS and the International Electrical Congress approved a new set of practical units for electricity and magnetism: the ohm for electrical resistance, the volt for the electromotive force, and the ampere for electric current. The schematic origins of Germany's Physikalisch-Technische Reichsanstalt (PTR)—the Imperial Physical Technical Institute for the Experimental Advancement of the Exact Sciences and Precision Technology—can be traced to an essay written by Karl Schellbach, "On the Foundations of a Museum for the Exact Sciences," published in 1872, a year after German unification. The renowned industrialist and engineer Ernst Werner von Siemens was responsible for the actualization of Schellbach's plan. In 1882 Siemens donated the building site that was to house the PTR. The German Reichstag officially approved the PTR on 28 March 1887. It originally comprised physics and technical departments. The physics department was composed of research laboratories for heat, electricity, and optics, while the technical department housed laboratories for precision metrology, heat, and pressure, as well as a second optical laboratory. The first president of the PTR was Germany's premier physicist, Hermann von Helmholtz.

The PTR not only served as the nation's leading metrological laboratory; its governing committee sought to forge links among scientists, engineers, instrument makers, private entrepreneurs, and government officials. In addition to Siemens and Helmholtz, other leading scientists on the advisory board of the PTR included Ernst Abbe, Rudolf Clausius, and Wilhelm Conrad Röntgen. From the very beginning the objectives of the PTR were fourfold: the execution of scientific experiments that necessitated the collaboration of teams of scientists and engineers; the testing and verification of the properties of materials used in precision-measuring devices; the testing and verification of the uniformity of the components used to produce precision-measuring devices; and the testing and verification of measuring tools.

From 1898 until 1945, the PTR was empowered by the Reichstag to provide the legal units of electricity and to monitor instruments for measuring electric current. In 1923 the Imperial Institute for Weights and Measures was integrated into the PTR, rendering the PTR the sole legal arbiter for monitoring calibration and testing offices. The PTR sustained heavy damage during World War II, and was rebuilt in 1946 as the office for the West Berlin Senate. Built in Brunswick in 1950, the Physikalisch-Technische Bundesanstalt (PTB) became the PTR's successor. The PTB, like the PTR, is totally state supported.

The PTR served as the model for the American National Bureau of Standards (NBS, now called the National Institute of Standards and Technology) founded in 1901 and the British National Physical Laboratory (NPL) founded in 1905. The NBS was the first physical science research laboratory funded by the U.S. government. Its directors have included some of the nation's leading physicists and engineers, including Samuel Wesley Stratton, Lyman J. Briggs, and Lewis M. Branscomb. Throughout its history, the NBS has undertaken research on a broad range of topics including electrical standards, aviation technology, uranium calibration research, atomic clocks, electronics, and parity. The NPL was created by the Cavendish physicist Richard Tetley Glazebrook. Starting out with a total of twenty-four physicists, the NPL had sixty-three by the outbreak of World War I. Enjoying less federal support than Germany's standards bureaus, the NPL and NBS have historically relied on a mix of government grants, testing fees, and (particularly in the case of the NPL) gifts from individuals and companies.

Perhaps the most important office of international weights and measures is the Bureau International des Poids et Mesures in France (BIPM). This agency ensures the international uniformity of standards. Its authority is granted by the Convention of the Meter, signed in Paris in 1895, which now represents the collaborative work of fifty-one member nations, including all industrialized countries. The BIPM, operating under the exclusive supervision of the International Committee for Weights and Measures, comprises committees whose members belong to the national meteorological laboratories of these member nations. The BIPM currently conducts research in seven principle areas: laser, wavelength, and frequency standards; mass; time; electricity; radiometry and photometry; ionizing radiation; and chemistry. It also undertakes research in thermometry, pressure, and humidity. During the eleventh Conférence Générale des Poids et Mesures in 1960, the International System of Units (SI) was officially recommended as the basis of scientific measurement. Its seven fundamental units are the meter, kilogram, second, ampere, kelvin, mole, and candela.

MYLES W. JACKSON